Approved Professional Information for Medicines for Human Use:

ZOLPIDEM 5 mg, 10 mg AUSTELL

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

ZOLPIDEM 5 mg AUSTELL 5 mg Film-coated tablets

ZOLPIDEM 10 mg AUSTELL 10 mg Film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZOLPIDEM 5 mg AUSTELL: Each film-coated tablet contains 5 mg zolpidem tartrate

ZOLPIDEM 10 mg AUSTELL: Each film-coated tablet contains 10 mg zolpidem tartrate

Contains sugar (lactose monohydrate).

Each 5 mg film-coated tablet contains 29,5 mg of lactose monohydrate

Each 10 mg film-coated tablet contains 59 mg of lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

ZOLPIDEM 5 mg AUSTELL

White to almost white, round, biconvex, film-coated tablets with ‘5’ embossing on one side and plain on the other side.

ZOLPIDEM 10 mg AUSTELL

White to almost white, caplet shaped, biconvex, film-coated tablets with break line on one side and '10' embossed on other side.

The score line is not intended for division of the tablet. The tablet should be swallowed whole.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- ZOLPIDEM AUSTELL is indicated for the short-term treatment of insomnia.
- ZOLPIDEM AUSTELL or a short acting hypnotic, is only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress.

4.2 Posology and method of administration

Posology

Treatment should be as short as possible. Generally, the duration of treatment varies from a few days to two weeks with a maximum, including the tapering off process, of four weeks.

In certain cases, extension beyond the maximum treatment period may be necessary; if so, it should not take place without re-evaluation of the patient's status.

ZOLPIDEM AUSTELL should be taken immediately before going to bed, or in bed.

ZOLPIDEM AUSTELL should be taken in a single intake and not be re-administered during the same night.

The recommended daily dose for adults is 10 mg immediately before bedtime, or in bed.

The lowest effective daily dose of ZOLPIDEM AUSTELL should be used and must not exceed 10 mg.

A lower dose of 5 mg is recommended for women (see section 4,7).

Special populations

Elderly population

Since elderly or debilitated patients may be especially sensitive to the effects of ZOLPIDEM AUSTELL, in these patients, a dose of 5 mg is recommended. The total ZOLPIDEM AUSTELL dose should not exceed 10 mg in this population.

Hepatic impairment

In patients with hepatic insufficiency, the recommended starting dose is 5 mg and particular caution must be exercised in elderly patients.

ZOLPIDEM AUSTELL is contraindicated in patients with severe hepatic insufficiency as it may precipitate encephalopathy (see section 4.3).

Paediatric population

Safety and effectiveness of ZOLPIDEM AUSTELL in paediatric patients under the age of 18 years have not been established. ZOLPIDEM AUSTELL should not be prescribed in this population. (see section 4.3).

Method of administration

ZOLPIDEM AUSTELL is for oral administration.

4.3 Contraindications

- Hypersensitivity to zolpidem or to any of the excipients of ZOLPIDEM AUSTELL listed in section 6.1.
- Myasthenia gravis.
- Sleep apnoea syndrome.
- Acute and/or severe respiratory insufficiency.
- Severe hepatic insufficiency (see section 4.4).
- Paediatric population under the age of 18.

- Safety in pregnancy and lactation has not been established (see section 4.6).

4.4 Special warnings and precautions for use

The cause of insomnia should be identified wherever possible and the underlying factors treated before ZOLPIDEM AUSTELL is prescribed. The failure of insomnia to remit after a 7 – 14 day course of treatment may indicate the presence of a primary psychiatric or physical disorder, and the patient should be carefully re-evaluated at regular intervals.

Next-day psychomotor impairment

Zolpidem, as in ZOLPIDEM AUSTELL has CNS-depressant effects. The risk of next-day psychomotor impairment, including impaired driving ability, is increased if:

- zolpidem tartrate is taken within less than 7 - 8 hours before performing activities that require mental alertness (see section 4.7)
- a dose higher than the recommended dose is taken
- zolpidem tartrate is co-administered with other CNS depressants or with other medicines that increase the blood levels of zolpidem tartrate, or with alcohol or illicit medicines (see section 4.5).

Zolpidem tartrate should be taken in a single intake immediately at bedtime and not be re-administered during the same night.

Specific patient groups

Respiratory insufficiency

As hypnotics have the capacity to depress respiratory drive, precautions should be observed if ZOLPIDEM AUSTELL is prescribed to patients with chronic respiratory insufficiency.

Hepatic insufficiency

ZOLPIDEM AUSTELL is contraindicated in patients with severe hepatic insufficiency as it may precipitate encephalopathy. (See section 4.2 and 4.3).

Elderly

See section 4.2 for dose recommendations.

Paediatric patients

ZOLPIDEM AUSTELL is contraindicated in patients under the age of 18 years (see section 4.3).

Risk from concomitant use of opioids

Concomitant use of zolpidem as in ZOLPIDEM AUSTELL and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines or related medicines such as zolpidem as in ZOLPIDEM AUSTELL with opioids should be reserved for patients for whom alternative treatment options are not possible.

If a decision is made to prescribe ZOLPIDEM AUSTELL concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section 4.2).

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their environment to be aware of these symptoms (see section 4.5).

Use in patients with a history of drug or alcohol abuse

Extreme caution should be exercised when prescribing for patients with a history of substance or alcohol abuse. These patients should be under careful surveillance when receiving zolpidem tartrate or any other hypnotic, since they are at risk of habituation and psychological dependence.

Psychotic illness

Hypnotics such as zolpidem in ZOLPIDEM AUSTELL are not recommended for the primary treatment of psychotic illness.

Suicidal ideation, suicide attempt, suicide and depression

Some epidemiological studies suggest an increased incidence of suicidal ideation, suicide attempt and suicide in patients with or without depression, and treated with benzodiazepines and other hypnotics, including zolpidem. However, a causal relationship has not been established.

Zolpidem tartrate should be administered with caution in patients exhibiting symptoms of depression. Suicidal tendencies may be present therefore the least amount of ZOLPIDEM AUSTELL that is feasible should be supplied to these patients to avoid the possibility of intentional overdose by the patient. Pre-existing depression may be unmasked during use of ZOLPIDEM AUSTELL. Since insomnia may be a symptom of depression, the patient should be re-evaluated if insomnia persists.

General information relating to effects seen following administration of benzodiazepines and other hypnotic medicines which should be taken into account by the prescribing physician are described below.

Tolerance

Some loss of efficacy to the hypnotic effects of short-acting benzodiazepines and benzodiazepine-like medicines like zolpidem as in ZOLPIDEM AUSTELL may develop after repeated use for a few weeks.

Dependence and abuse

Use of zolpidem may lead to the development of abuse and/or physical and psychological dependence. The risk of dependence increases with dose and duration of treatment. The risk of abuse and dependence is also greater in patients with a history of psychiatric disorders and/or alcohol, substance or medicine abuse. Zolpidem should be used with extreme caution in patients with current or a history of alcohol, substance or medicine abuse or dependence.

If physical dependence is developed, a sudden discontinuation of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.
Sedatives/hypnotics including zolpidem as in ZOLPIDEM AUSTELL have produced withdrawal signs and symptoms following abrupt discontinuation. These symptoms range from mild dysphoria and insomnia to a withdrawal syndrome that may include abdominal and muscle cramps, vomiting, sweating, tremors and convulsions. The following adverse events have been reported: fatigue, nausea, flushing, light-headedness, uncontrolled crying, emesis, stomach cramps, panic attack, nervousness and abdominal discomfort.

Rebound insomnia

A transient syndrome whereby the symptoms that led to treatment with a benzodiazepine or benzodiazepine-like medicine recur in an enhanced form may occur on withdrawal of hypnotic treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness.
It is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms should they occur when the medicine is discontinued. Since the risk of withdrawal phenomena or rebound has been shown to be greater after abrupt discontinuation of treatment, it is recommended that the dosage is decreased gradually where clinically appropriate.
There are indications that, in the case of benzodiazepines and benzodiazepine-like medicines with a short duration of action, such as zolpidem as in ZOLPIDEM AUSTELL withdrawal phenomena can become manifest within the dosage interval.

Amnesia

Benzodiazepines or benzodiazepine-like medicines such as zolpidem in ZOLPIDEM AUSTELL may induce anterograde amnesia. The condition occurs most often several hours after ingesting the ZOLPIDEM AUSTELL. In order to reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 7 - 8 hours (see section 4.8).

Other psychiatric and "paradoxical" reactions

Other psychiatric and paradoxical reactions like restlessness, exacerbated insomnia, agitation, irritability, aggression, delusion, anger, nightmares, hallucinations, psychosis, abnormal behaviour and other adverse behavioural effects are known to occur when using benzodiazepines or benzodiazepine-like medicines such as zolpidem in ZOLPIDEM AUSTELL. Should this occur, use of the product should be discontinued. These reactions are more likely to occur in the elderly (see section4.8).

Somnambulism and associated behaviours

Sleep walking and other associated behaviours such as "sleep driving, preparing and eating food, making phone calls or having sex, with amnesia from the event, have been reported in patients who had taken zolpidem as in ZOLPIDEM AUSTELL and were not fully awake.

The use of alcohol and other CNS-depressants with zolpidem as in ZOLPIDEM AUSTELL appears to increase the risk of such behaviours, as does the use of ZOLPIDEM AUSTELL at doses exceeding the maximum recommended dose. Discontinuation of ZOLPIDEM AUSTELL should be strongly considered for patients who report such behaviours (for example, sleep driving), due to the risk to the patient and others (see sections 4.5 and 4.8).

Severe injuries

Due to its pharmacological properties, zolpidem can cause drowsiness and a decreased level of consciousness, which may lead to falls and consequently to severe injuries.

Duration of treatment

The duration of treatment should be as short as possible and should not exceed 4 weeks, including the tapering off process. Extensions beyond these periods should not take place without re-evaluation of the situation.

It may be useful to inform the patient when treatment is started that it will be of limited duration, and to explain precisely how the dosage will be progressively decreased.

Patients with long QT syndrome

An in vitro cardiac electrophysiological study showed that under experimental conditions using very high concentration and pluripotent stem cells zolpidem may reduce the hERG (human ether-a-go-gorelated gene) related potassium currents. The potential consequence in patients with congenital long QT syndrome is unknown. As a precaution, the benefit/risk ratio of zolpidem as in ZOLPIDEM AUSTELL treatment in patients with known congenital long QT syndrome should be carefully considered.

Excipients: lactose intolerance

ZOLPIDEM AUSTELL contains lactose monohydrate.

Patients with rare hereditary problems of galactose intolerance, total Lapp lactase deficiency or glucose-galactose malabsorption should not take this ZOLPIDEM AUSTELL.

4.5 Interaction with other medicines and other forms of interaction

Not recommended

Concomitant intake with alcohol

The sedative effect of zolpidem may be enhanced when ZOLPIDEM AUSTELL is used in combination with alcohol. This affects the ability to drive or use machines.

Take into account

Combination with CNS depressants

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant medicines, narcotic analgesics, antiepileptic medicines, anaesthetics and sedative antihistamines. Therefore, concomitant use of zolpidem, as in ZOLPIDEM AUSTELL with these medicines may increase drowsiness and next-day psychomotor impairment, including impaired driving ability (see sections 4.4 and 4.7). Also, isolated cases of visual hallucinations were reported in patients taking zolpidem with antidepressants including bupropion, desipramine, fluoxetine, sertraline and venlafaxine.

Co- administration of fluvoxamine may increase blood levels of zolpidem tartrate, concurrent use is not recommended (see CYP450 inhibitors and inducers).

In the case of narcotic analgesics enhancement of euphoria may also occur leading to an increase in psychological dependence.

Opioids

The concomitant use of sedative medicines such as benzodiazepines or related medicines such as zolpidem, as in ZOLPIDEM AUSTELL with opioids increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

CYP450 inhibitors and inducers

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines and benzodiazepine-like medicines like zolpidem.
Zolpidem tartrate is metabolised via several hepatic cytochrome P450 enzymes, the main enzyme being CYP3A4 with the contribution of CYP1A2. The pharmacodynamic effect of zolpidem tartrate is

decreased when it is administered with a CYP3A4 inducer such as rifampicin and St. John's Wort. St. It was reported that St. John's Wort has been shown to have a pharmacokinetic interaction with zolpidem. Mean Cmax and AUC were decreased (33,7 % and 30,0 % lower, respectively) for zolpidem administered with St. John's Wort compared to zolpidem administered alone. Co-administration of St. John's Wort may decrease blood levels of zolpidem, concurrent use is not recommended.

However, when zolpidem tartrate was administered with itraconazole (a CYP3A4 inhibitor) its pharmacokinetics and pharmacodynamics were not significantly modified. The clinical relevance of these results is unknown. Co-administration of zolpidem as in ZOLPIDEM AUSTELL with ketoconazole (200 mg twice daily), a potent CYP3A4 inhibitor, prolonged zolpidem elimination half-life, increased total AUC, and decreased apparent oral clearance when compared to zolpidem plus placebo. The total AUC for zolpidem, when co-administered with ketoconazole, increased by factor of 1,83 when compared to zolpidem alone. A routine dosage adjustment of zolpidem is not considered necessary, but patients, should be advised that use of zolpidem with ketoconazole may enhance the sedative effects.

Since CYP3A4 plays an important role in zolpidem tartrate metabolism, possible interactions with medicines that are substrates or inducers of CYP3A4 should be considered.

Fluvoxamine is a strong inhibitor of CYP1A2 and a moderate to weak inhibitor of CYP2C9 and CYP3A4. Co-administration of fluvoxamine may increase blood levels of ZOLPIDEM AUSTELL, concurrent use is not recommended.

Ciprofloxacin has been shown to be a moderate inhibitor of CYP1A2
and CYP3A4. Co-administration of ciprofloxacin may increase blood levels of zolpidem tartrate, concurrent use is not recommended.

Other medicines

When zolpidem tartrate was administered with warfarin, digoxin, cimetidine or ranitidine, no significant pharmacokinetic interactions were observed.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been demonstrated (see section 4.3).

Women of childbearing potential

If zolpidem is prescribed to a woman of childbearing potential, she should be warned to contact her doctor about stopping the ZOLPIDEM AUSTELL if she intends to become or suspects that she is pregnant.

Pregnancy

The use of zolpidem during pregnancy should be avoided.

Zolpidem crosses the placenta.

A large amount of data on pregnant women (more than 1000 pregnancy outcomes) collected from cohort studies has not demonstrated evidence of the occurrence of malformations following exposure to benzodiazepines or benzodiazepine-like substances during the first trimester of pregnancy. However, certain case-control studies reported an increased incidence of cleft lip and palate associated with use of benzodiazepines during pregnancy.

Cases of reduced fetal movement and fetal heart rate variability have been described after administration of benzodiazepines or benzodiazepine-like substances during the second and /or third trimester of pregnancy.

Administration of zolpidem during the late phase of pregnancy or during labour has been associated with effects on the neonate, such as hypothermia, hypotonia, feeding difficulties (‘floppy infant syndrome’) and respiratory depression due to the pharmacological action of zolpidem. Cases of severe neonatal respiratory depression have been reported.

Moreover, infants born to mothers who took sedative /hypnotics-medicines such as zolpidem as in ZOLPIDEM AUSTELL chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk of developing withdrawal symptoms in the postnatal period. Appropriate monitoring of the newborn in the postnatal period is recommended.

Breastfeeding

Small quantities of zolpidem tartrate appear in breast milk. The use of zolpidem tartrate in nursing mothers is therefore contraindicated (see section 4.3).

4.7 Effects on ability to drive and use machines

ZOLPIDEM AUSTELL has major influence on the ability to drive and use machines.

Vehicle drivers and machine operators should be warned that, there may be a possible risk of drowsiness, prolonged reaction time, dizziness, sleepiness, blurred /double vision and reduced alertness and impaired driving the morning after therapy (see section 4.8). In order to minimise this risk a lower dose is recommended for women and a resting period of at least 8 hours is recommended between taking ZOLPIDEM AUSTELL and driving, using machinery and working at heights.

Driving ability impairment and behaviours such as 'sleep-driving' have occurred with zolpidem tartrate, as in ZOLPIDEM AUSTELL alone at therapeutic doses.

Furthermore, the co-administration of zolpidem tartrate, as in ZOLPIDEM AUSTELL with alcohol and other CNS depressants increases the risk of such behaviours (see sections 4.4 and 4.5). Patients should be warned not to use alcohol or other psychoactive substances when taking ZOLPIDEM AUSTELL.

4.8 Undesirable effects

There is evidence of a dose-relationship for adverse effects associated with zolpidem tartrate use, particularly for certain CNS and gastrointestinal events. As recommended in section 4.2, they should in theory be less if zolpidem tartrate is taken immediately before retiring, or in bed. They occur most frequently in elderly patients.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations	Upper respiratory tract infection, lower respiratory tract infection		
Immune system disorders			Angioedema
Metabolism and nutrition disorders		Appetite disorder	
Psychiatric disorders *	Hallucination, agitation, nightmare, depression (see section 4.4)	Confusional state, irritability, restlessness, aggression, somnambulism (see section 4.4), euphoric mood, libido disorder	Anger, psychosis, abnormal behaviour

		delusion, dependence (withdrawal symptoms, or rebound effects may occur after treatment discontinuation)	
Nervous system disorders	Somnolence, headache, dizziness, exacerbated insomnia, cognitive disorders such as anterograde amnesia (amnestic effects may be associated with inappropriate behaviour)	Paraesthesia, tremor, disturbance in attention, speech disorder depressed level of consciousness	
Eye disorders		Diplopia, vision blurred visual impairment	
Respiratory, thoracic and mediastinal disorders		Respiratory depression (see section 4.4)	
Gastrointestinal disorders	Diarrhoea, nausea, vomiting, abdominal pain		
Hepatobiliary disorders		Liver enzymes elevated	

		hepatocellular, cholestatic or mixed liver injury (see sections 4.2, 4.3 and 4.4)	
Skin and subcutaneous tissue disorders		Rash, pruritus, hyperhidrosis urticaria	
Musculoskeletal and connective tissue disorders	Back pain	Myalgia, muscle spasms, muscular weakness, arthralgia, neck pain	
General disorders and administration site conditions	Fatigue	Gait disturbance, fall (predominantly in elderly patients and when zolpidem was not taken in accordance with prescribing recommendation) (see section 4.4).	Drug tolerance

* Most of these psychiatric undesirable effects are related to paradoxical reactions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms

In cases of overdose involving zolpidem tartrate alone or with other CNS-depressant medicines (including alcohol), impairment of consciousness ranging from somnolence to coma, and more severe symptomatology, including fatal outcomes have been reported.

Treatment

General symptomatic and supportive measures should be used. Activated charcoal should be given to reduce absorption. Sedating medicines should be withheld even if excitation occurs. Benzodiazepine-antagonists, such as flumazenil, may be considered where serious symptoms are observed. Flumazenil is reported to have an elimination half-life of about 40 – 80 minutes. Patients should be kept under close observation because of this short duration of action; further doses of flumazenil may be necessary. However, flumazenil administration may contribute to the appearance of neurological symptoms (convulsions).

Zolpidem is not dialyzable. The value of dialysis in the treatment of an overdose has not been determined. Dialysis in patients with renal failure receiving therapeutic doses of zolpidem have demonstrated no reduction in levels of zolpidem.

In the management of overdose with any medicine, it should be borne in mind that multiple medicines may have been taken.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 2.2. Sedatives, hypnotics

Pharmacotherapeutic group: Benzodiazepine related drugs

ATC Code: N05CF02

(GABA-A receptor modulator selective for omega-1 receptor subtype hypnotic agent).

Zolpidem is an imidazopyridine compound with sedative/hypnotic effects. These effects are related to a specific agonist action at central receptors belonging to GABA-omega benzodiazepine-1 and benzodiazepine-2 macromolecular receptor complex, modulating the opening of the chloride ion channel. Zolpidem acts primarily upon the omega-1 (benzodiazepine-1) receptor subtypes. The clinical relevance of this is not known.

Paediatric population

Safety and efficacy of zolpidem have not been established in children aged less than 18 years.

5.2 Pharmacokinetic properties

Absorption

After oral administration, the bioavailability of zolpidem is about 70 %, reaching peak plasma concentration between 0,5 and 3 hours after dosing.

Distribution

At therapeutic dose levels, the pharmacokinetics are linear. The degree of plasma protein binding is about 92 %. The plasma elimination half-life is about 2,5 hours (1,4 - 3,8 hours). The distribution volume in adults is 0,54 ± 0,02 L /kg. The distribution volume decreases to 0,34 ± 0,05 L /kg in the very elderly.

Elimination

Zolpidem is excreted in the form of inactive metabolites (hepatic metabolism), mainly in the urine (56 %) and faeces (37 %). It has no inducing effects on hepatic enzymes.

Special populations

In elderly subjects, clearance is reduced. The peak concentration is increased by about 50 % and elimination half-life by 32 %.

In patients with renal insufficiency, whether dialysed or not, there is a moderate reduction in clearance. The other pharmacokinetic parameters are unaffected.

In patients with hepatic insufficiency, the bioavailability of zolpidem is increased. Clearance is reduced and the elimination half-life prolonged (about 10 hours).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Pregelatinised starch

Silica colloidal anhydrous

Sodium starch glycollate

Film coating:

Hypromellose

Macrogol 6000

Talc

Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 ºC.

6.5 Nature and contents of container

ZOLPIDEM AUSTELL 5 mg and 10 mg film-coated tablets are packed in clear PVC / Aluminium blisters packs of 10 film-coated tablets. The blisters are then packaged in an outer carton containing 10, 20 or 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBERS

ZOLPIDEM 5 mg AUSTELL: 50/2.2/0218

ZOLPIDEM 10 mg AUSTELL: 50/2.2/0219

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 July 2022

10. DATE OF REVISION OF THE TEXT